

# Global Atmospheric Change and Research Needs in Environmental Health Sciences

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## Introduction

On November 6-7, 1989, the National Institute of Environmental Health Sciences (NIEHS) held a conference on Global Atmospheric Change and Human Health. As a result, and in the months since this conference, many important areas of research have been identified with regard to the impacts of climatic changes on human health. To develop comprehensive research programs that address important human health issues related to global warming, it is necessary to begin by recognizing that some of the health effects will be direct such as those due to temperature changes, and others will be indirect consequences of environmental alterations resulting in crop loss, changing disease vectors, population migration, etc. It should also be recognized that the conditions leading to global warming have importance to human health and the environment other than through increasing concentrations of CO<sub>2</sub> in the atmosphere, rising surface temperatures, and rising sea levels. Much of the increase in CO<sub>2</sub> in the atmosphere is due to the increased combustion of fossil fuels for transportation and electric power production. Over the next 30 years, the demand for electrical power is expected to grow at a rate of 2 to 4% per year in the United States alone, and even faster growth is likely for developing countries. Much of this energy will be derived from the combustion of fossil fuels, including coal, which result in pollutant emissions to the air such as metals, radioactivity, SO<sub>x</sub>, NO<sub>x</sub>, and particles. Therefore, with increasing concentrations of CO<sub>2</sub> there will not only be the effects of global warming on health, but also increasing concentrations of many serious air pollutants in urban areas, includ-

ing the precursors of acid rain and acid deposition over large regional areas. The chlorofluorocarbons (CFCs) also contribute to global warming because of their strong absorbance of infrared radiation. Of significance is the long residence times of the CFCs in the troposphere and their capacity to photodegrade in the stratosphere, producing free radicals that react with ozone. The continued depletion of the protective ozone layer in the stratosphere allows increased exposure of all life to shorter wavelength ultraviolet radiation.

The order in which recommendations for future research are presented is not meant to establish priorities. The purpose is to emphasize the interrelated and interconnected nature of environmental processes that affect global atmospheric change and how they influence exposure to toxic chemicals.

## Geophysics of Global Climatic Change

There is a great need to be able to predict more accurately how changes in greenhouse gases affect climate, surface temperatures, and rainfall amounts not only on a global scale but for small geographical areas as well. For global warming models to be more accurate, a much better understanding of global and regional climatic processes must be obtained, and the affects of oceans and clouds must be incorporated into these models in a more realistic manner.

There is still much that is not known about the impacts of global climate change on human health. Therefore, it is important to continue to investigate individually the various phenomena that contribute to climatic/health changes. These include stratospheric ozone depletion, global warming, acid aerosol and photochemical oxidant formation, desertification, and deforestation. It is important to understand the dynamics of these processes on global, continental, and regional scales. However, these processes are happening concurrently and interactively. Although it is sometimes helpful to divide a problem into components in order to analyze what contributions are made by the various pieces, at some point the parts must be reassembled

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and analyzed for the sum total of the effects. Global climate change models have not been used directly to determine the impacts of climatic change on human health. In addition, more study is needed of the impacts of climatic changes on other important areas such as agriculture and natural resources which can indirectly affect human health.

## Replacement Chemicals for the CFCs

**Atmospheric Chemistry.** Global warming potentials and ozone-depleting capacities of many replacement chemicals for the CFCs are incomplete. The hydrochlorofluorocarbons (HCFCs) appear to be the most likely candidates to replace the CFCs because they degrade much faster than the CFCs in the troposphere. However, their degradation products need to be better characterized chemically and biologically, and the parent chemicals, the HCFCs, need to be better characterized toxicologically. Many of the HCFCs have molecular structures similar to the anesthetic halothane (toxic to liver, kidney, cardiovascular, and central nervous systems).

**Toxicology.** *In vivo* toxicity studies on HCFCs should include short- and long-term toxicity studies, including, at least, developmental and reproductive toxicity, neurotoxicity, carcinogenic potential, mutagenicity, and immunotoxicity. Toxicity studies in *in vitro* systems should include mutagenicity studies in submammalian test systems and should explore possible mechanisms of toxicity.

Future studies should examine fully the extent and nature of the interactions of HCFC metabolites with cellular macromolecules because modifications of cellular macromolecules may be associated with carcinogenesis/cytotoxicity. Because the analog 2-chloro-2,2-difluoroethanol is a metabolite of HCFC-132a, future studies might address the potential toxicity of 2,2,2-trihaloethanol metabolites of HCFCs.

**Metabolism.** Limited metabolic data are available for most HCFCs proposed as replacements for CFCs. Hence metabolism studies should include investigations on the pharmacokinetics of uptake and elimination of HCFCs as well as investigations on the *in vivo* metabolic fate of HCFCs, including identification of metabolites, their possible interaction with cellular constituents, and the mechanisms and routes of clearance of metabolites. *In vitro* metabolism studies should be used to identify *a*) target organs; *b*) the enzymes catalyzing the metabolism of HCFCs; *c*) possible associations between metabolism and toxicity; and *d*) interactions of HCFC metabolites with cellular macromolecules. Because the HCFCs constitute a group of closely related analogs, computational analysis of data from these and other structure metabolism studies may be used to improve predictability of the metabolic fate of HCFCs, interactions of HCFC metabolites with cellular macromolecules, and relationships between HCFC metabolism and toxicity.

## Exposure to Mixtures of Air Pollutants

Important conclusions from the exposure studies with mixtures of ozone and acid aerosols provide examples of studies that need to be conducted on all air pollutants. These conclusions are *a*) ozone-acid aerosol interactions occur in rats at concentrations of each agent that approximate actually encountered ambient levels; *b*) several sensitive assays may be used to quantify the

acute response of the lung to oxidants, alone and in combination with respirable acid aerosols; *c*) there is a reasonably good correlation between the most sensitive biochemical and morphometric indicators of lung response studied; and *d*) acidity of an aerosol is apparently a necessary and sufficient condition for it to interact synergistically with an oxidant gas to cause increased lung damage. The acidic aerosol most likely to occur in polluted air is ammonium sulfate or bisulfate.

Using these studies as a beginning, continued research on indoor and outdoor exposure to air pollutants should continue along the following lines.

**Determining Cumulative Exposures to Air Pollutants in Indoor and Outdoor Environments.** Programs are needed to determine how concentrations of air pollutants change as a result of weather conditions, atmospheric chemistry, and the characteristics of homes and buildings. In addition, programs should continue to determine in a more precise manner how much time people spend in different environments. Cumulative and instantaneous exposures to indoor and outdoor air pollutants are the product of the concentrations of these pollutants as functions of time multiplied by the period of time that the person spends in a particular environment. Along with exposure to air pollutants found outdoors (e.g., CO, particles, NO<sub>x</sub>, acid aerosols, SO<sub>2</sub>, and O<sub>3</sub>), special indoor sources of pollutants include tobacco smoke, volatile organic chemicals used in building materials, volatile organic chemicals from household solvents, radon, lead and other toxic metals, asbestos, biological contaminants, allergens, and exhaust emissions from gas stoves and kerosene heaters. Research should also continue on developing personal exposure monitors that are capable of measuring cumulative exposures to individual and multiple air pollutants.

**Determining Relationships between Measured Concentrations and Doses Delivered to the Lung, Other Internal Organs, and Other Tissues.** Some of the problems of dosimetry can be addressed with physiologically based pharmacokinetic studies. These studies combine efforts in basic physiology, metabolism, uptake, and distribution of inhaled pollutants. Most of these studies have been confined to single chemical exposures, but future studies should continue to examine the interactions that result from multiple chemical exposures (concomitant and sequential).

**Determining the Human Health Risks from Exposure to Air Pollutants.** Questions to be addressed in these studies include determining molecular and cellular biomarkers of exposure; determining which tissues are damaged; how much damage is required before disease appears in populations with different levels of sensitivity (e.g., children, elderly people, people with chronic respiratory and cardiovascular diseases, and people with compromised immune systems who are more susceptible to bacterial and viral diseases); and determining the relationships between exposures to and biomarkers for mixtures of air pollutants and health effects in differing members of a population (e.g., normal healthy people, children, elderly people, people with chronic respiratory and cardiovascular diseases, and people with compromised immune systems). In this regard greater attention must be given to determining advantages and limitations of the use of biomarkers in identifying susceptible populations and in epidemiological studies. Important research questions in this regard are validation of biomarkers; reducing ambiguities in

many biomarkers (e.g., specificity/sensitivity); reducing variability in biomarkers; and continued efforts to establish more links between quantification of exposure with biomarkers and well-defined health effects.

## Acid Deposition and Bioavailability of Metals

Along with the direct (usually pulmonary) effects of acid aerosols on human health, acid aerosols and acid rain precursors also are important in increasing the bioavailability in soils and sediments of toxic metals such as mercury, lead, cadmium, arsenic, and aluminum. Inorganic forms of mercury are more readily transformed into the highly toxic organomercury compound methylmercury when conditions become more acidic in water, soils, and sediments. Human exposure to methylmercury compounds, in particular, is almost exclusively from the consumption of fish and fish products. Consumption of marine/freshwater fish, shellfish, etc., is an important source of exposure to methylmercury for certain human/animal populations.

Methylmercury affects primarily the central nervous system. In severe poisoning cases in adults, specific anatomical areas of the brain are permanently damaged. The first symptom of mercury damage at the lowest doses are complaints of paresthesias—an abnormal sensation or loss of sensation in the extremities of the hands and feet and circumorally. Prenatal life is more susceptible to brain damage from methylmercury as compared with the adult. Methylmercury is believed to inhibit cellular organizational processes basic to cell division and neuronal migration. Cases of severe exposure prenatally can result in massive disruption of the developing brain.

These studies need to be extended to other toxic metals to determine what factors associated with global warming affect increased mobility of metals in the environment, increased bioaccumulation in foods, etc., and health effects resulting from consumption of these accumulations.

## Biodiversity, Ecosystem Dynamics, and Spread of Infectious Disease

Climatic changes may produce large changes in ecosystem dynamics, populations, and biodiversity. These changes in ecology and ecosystem dynamics may be particularly important for the spread of infectious diseases. The spread of dengue, yellow fever, and cholera will probably be stimulated by climatic warming changes. The spread of other infectious diseases will also be affected. Predictions of the effects of global warming include relatively severe modifications of some forest habitats. As these habitats change/decline, so will many of the more fragile species of insect vectors and vertebrate hosts of parasitic, bacterial, and viral infections. As a result, there may be a gradual decline in prevalence of LaCrosse encephalitis virus which depends in part on tree-holes of hardwood forests for breeding of its vector, *Aedes triseriatus*, and for maintenance of its vertebrate hosts, squirrels and chipmunks. Also, we may see a decline in Lyme disease, caused by *Borrelia burgdorferi*, a spirochete transmitted by the tick, *Ixodes*

*dammini*. Tick populations are dependent in their adult stage on deer for their blood meals (although deer population reduction does not always lead to reduced tick populations), and deer populations are dependent at least in part on forests for browsing and cover.

New infectious diseases may emerge as a result of climatic changes caused by global warming. The agents of such diseases are not actually new. They have been present in natural wildlife cycles, and it is the ecology that changes, bringing the agent in contact with humans. The relatively rapid ecologic changes related to global warming that are now predicted can cause this process to be accelerated. As change occurs, creatures extend their distribution and overlap occurs. In the special case of segmented genome viruses, ecological overlap of populations creates an abundant opportunity for reassortment of genes, which could increase the virulence of the progeny virus. There is no way to anticipate these events, but their potential argues for maintenance of a strong biomedical monitoring/research infrastructure and a close watch for new diseases. From past experience, diseases such as cholera have the potential to become epidemic when the water ecology changes and temperatures rise. For this reason, research is needed to understand better the relationship between various ecological factors (e.g., temperature, humidity, and population diversity) and the generation of epidemics of each disease.

These ecological studies should be multidisciplinary, involving botany (including forestry), zoology, entomology, microbiology, hydrology, climatology, and epidemiology. The information required to project what will happen with climate change can best be acquired in the field, studying survival and adaptation especially at the fringe of the distribution of species of plants, vertebrate animals, and arthropods. Confirmatory laboratory studies will also be needed, especially of arthropod vectors and the interaction of infectious agents with the vector. These laboratory studies should examine factors such as survival of the vector and infectious agent as functions of changes in temperature and humidity and ability of the agent to multiply or go through its development cycle in the vector under changed conditions. The ecology of water systems that harbor cholera organisms should also be studied. With the information gained, it might be possible to project better what will happen with specific diseases after selected global climate changes.

In addition, more research is needed on ways to control vectors. Whatever climate and ecologic change occurs, it is likely to result in an increase in some vector-borne diseases. The only generic defense (other than health education) will be control of vectors. Studies on the delayed/chronic, low-level toxicity/human health effects of new pesticides are examples of needed research.

## Depletion of the Ozone Layer/Greater Exposure to UV Radiation

The CFCs are not only important greenhouse gases, but because of their long half-lives in the atmosphere, they are estimated to continue to deplete the ozone layer in the stratosphere for the next 40 to 50 years. Depletion of the ozone layer will allow shorter wavelength ultraviolet radiation (UVR) to

to reach the earth's surface. Relation between increased exposure to UV-B (wavelengths between 280 and 320 nm) and shorter UV wavelength radiation and possible increases in nonmelanoma and melanoma skin cancers are still areas of research that are not totally resolved with regard to dose response. Research on the relation between increased exposure to UVR and various ocular dysfunction also requires additional research.

In recent years, evidence has accumulated in animal model studies that exposure to high doses of UV-B radiation produces selective alterations in immune function that are mainly evidenced in the form of suppression of normal delayed-type cutaneous immune responses. In animals, this immune suppression is important for the development of nonmelanoma skin cancer and may influence the development and course of infectious diseases and possibly protect against autoimmune reactions. The evidence that UVR-induced cutaneous immune suppression occurs in humans is incomplete and needs to be investigated further. Along with studies in animals, studies are required to establish whether UV-B radiation can cause suppression of immune function in humans; determine whether melanin pigmentation can provide protection against such suppression; determine the role of such suppression in the pathogenesis of human skin cancer; determine whether UV-B can affect the development of infectious diseases (e.g., leishmaniasis) and vaccine effectiveness; determine if UV-B can produce photosensitivity and photoallergic responses in people requiring continuous long-term drug treatment for chronic illnesses; and determine whether UV-B can affect the capacity for human skin to develop protective mechanisms that can limit such damage.

## Global Warming Solutions— Unanswered Questions

Unresolved issues have already been identified for the replacement chemicals for the CFCs, but other unresolved environmental health issues relate to methods to reduce the combustion of fossil fuels and emissions of CO<sub>2</sub>. Various "oxygenated" and nonhydrocarbon fuels for automobiles have been proposed as a method to reduce urban air pollution and reduce emissions of acid rain precursors. It is important to characterize the exhaust emissions from these alternative fuels both chemically and biologically and to determine the health effects of exhaust emissions from both well-tuned and untuned automotive engines. Photovoltaic devices are attractive energy alternatives that convert sunlight directly into electricity. Because there is no combustion of fossil fuels in this electricity production process, CO<sub>2</sub> concentrations in the atmosphere should drop. Several of the more efficient photovoltaic/solar cell designs use Group III and Group V elements from the Periodic Chart of Elements. Elements such as arsenic, gallium, indium, antimony, and thallium belong to these groups of elements. Except for arsenic, toxicity data on these elements are incomplete.

The increased use of nuclear power plants to generate electricity has also been proposed as a method of reducing global warming because there is no release of CO<sub>2</sub> and other common air pollutants during energy generation. The recent disaster at the Chernobyl nuclear power plant in the Soviet Union indicates that more work is needed to make this technology as fail-safe as possible. There is also a need to develop an agreed-on procedure to dispose of or recycle spent fuels rods from these power plants.